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REVIEW

Safety and efficacy of second-generation drug-eluting stents compared with bare-metal stents: An updated meta-analysis and regression of 9 randomized clinical trials

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The efficacy of second-generation drug-eluting stents (DES; eg, everolimus and zotarolimus) compared with bare-metal stents (BMS) in patients undergoing percutaneous coronary intervention was challenged recently by new evidence from large clinical trials. Thus, we aimed to conduct an updated systematic review and meta-analysis of randomized clinical trials (RCTs) evaluating the efficacy and safety of second-generation DES compared with BMS. Electronic databases were systematically searched for all RCTs comparing second-generation DES with BMS and reporting clinical outcomes. The primary efficacy outcome was major adverse cardiac events (MACE); the primary safety outcome was definite stent thrombosis. The DerSimonian and Laird method was used for estimation of summary risk ratios (RR). A total of 9 trials involving 17 682 patients were included in the final analysis. Compared with BMS, second-generation DES were associated with decreased incidence of MACE (RR: 0.78, 95% confidence interval [CI]: 0.69-0.88), driven by the decreased incidence of myocardial infarction (MI) (RR: 0.67, 95% CI: 0.48-0.95), target-lesion revascularization (RR: 0.47, 95% CI: 0.42-0.53), definite stent thrombosis (RR: 0.57, 95% CI: 0.41-0.78), and definite/probable stent thrombosis (RR: 0.54, 95% CI: 0.38-0.80). The incidence of all-cause mortality was similar between groups (RR: 0.94, 95% CI: 0.79-1.10). Meta-regression showed lower incidences of MI with DES implantation in elderly and diabetic patients ($P = 0.026$ and $P < 0.0001$, respectively). Compared with BMS, second-generation DES appear to be associated with a lower incidence of MACE, mainly driven by lower rates of target-lesion revascularization, MI, and stent thrombosis. However, all-cause mortality appears similar between groups.

KEYWORDS

Coronary Artery Disease, Drug-Eluting Stents, Percutaneous Coronary Intervention

1 | INTRODUCTION

Since the introduction of coronary angioplasty, percutaneous coronary intervention (PCI) has advanced rapidly from plain-old balloon angioplasty to first- and then second-generation drug-eluting stents (DES). Compared with bare-metal stents (BMS), DES were developed to decrease the rate of clinically significant stent complications such as restenosis after PCI.[1] However, first-generation DES were also associated with increased risk of late stent thrombosis and death, especially with discontinuing dual antiplatelet therapy (DAPT) early.[2–4] Second-generation DES aimed to improve the DES safety profile. Meta-analyses thus far have been limited in patient numbers and/or duration of follow-up when comparing second-generation DES with BMS.[5–7] The recently published Norwegian Coronary Stent

(NORSTENT) trial was a randomized controlled trial (RCT) that included >9000 patients and adds significant new data for analysis. This trial suggested that there was no difference in the risk of death and MI between second-generation DES and BMS. However, some authors had argued that the NORSTENT trial was underpowered to detect a difference between devices.[8] Thus, we aimed to further evaluate the safety and efficacy of second-generation DES via comprehensive meta-analysis.

2 | METHODS

2.1 | Data sources and study selection

A detailed search of electronic databases, including MEDLINE, Web of Science, and Cochrane Central Register of Controlled Trials, was conducted from inception until March 2017 for all RCTs comparing second-generation DES (eg, zotarolimus or everolimus DES) with BMS, without language restrictions. The following keywords were used: "everolimus," "zotarolimus," "bare metal," and "stent." The search was restricted to RCTs on humans. The references of the included trials were also screened for trials not included by the search strategy. The current meta-analysis was conducted in concurrence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9] We excluded trials comparing biodegradable-polymer DES with BMS, given the different duration of DAPT recommended for these stents and different patient population (ie, patients with higher risk of bleeding) that could affect the outcomes assessed in our study.

2.2 | Data extraction

Two independent reviewers (NS and AYE) extracted the data regarding each study's baseline characteristics and patient characteristics, quality of the included studies, and all outcomes of interest. Two different authors (ANM and IYE) crosschecked the collected data to ensure its accuracy. All outcomes events were tabulated, preferably by the longest follow-up duration.

2.3 | Outcomes and definitions

The primary efficacy outcome of interest was major adverse cardiac events (MACE) as defined by each study. The primary device safety outcome was stent thrombosis (definite and definite/probable). Secondary outcomes were all-cause mortality, myocardial infarction (MI; defined as any MI), and target-lesion revascularization (TLR). We collected target-vessel MI whenever reported. (See Supporting Information, Table 1, in the online version of this article for the definitions of MACE as reported in the individual studies.)

2.4 | Quality assessment

Quality assessment was established on both the study level, using the Cochrane risk of bias tool,[10] and individual outcome level, using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool.[11] Both tools were used in prior similar publications and have been explained in further detail previously.[12]

2.5 | Statistical analysis

All descriptive analyses were conducted using weighted frequencies for the categorical variables and weighted means and SDs for continuous ones. Random-effects weighted incidences were calculated for all outcomes of interest using Stata software (Metaprop), and all statistical analysis was performed using Stata software, version 14 (StataCorp LP, College Station, TX). Summary random-effects risk ratios (RR) with 95% confidence intervals (CI) were calculated for all outcomes of interest using the DerSimonian and Laird model.[13] The I^2 statistic was used for evaluation of in-between studies heterogeneity with values of 0% to 30%, >30% to 60%, and >60% corresponding to low, moderate, and high degrees of heterogeneity, respectively.[14] Publication bias was assessed using the Egger method, with a P value <0.05 corresponding to positive evidence of publication bias.[15]

Further sensitivity and meta-regression analyses were conducted for further exploration of the reasons for heterogeneity in the outcomes with moderate to high degree of heterogeneity. These analyses were conducted according to the percentage of left anterior descending (LAD) artery involvement, percentage of patients with diabetes mellitus (DM), and the mean age of the patients included in each study. A sensitivity analysis was conducted after exclusion of trials with different definitions of MACE and trials with different durations of DAPT in both arms. Finally, subgroup analysis according to the stent type was performed for both primary safety and efficacy outcomes. A 2-sided P value of <0.05 and CI of 95% was considered statistically significant.

3 | RESULTS

3.1 | Studies included and patients' characteristics

The initial search resulted in 262 records, out of which 249 were excluded after reviewing the titles and abstracts. Fourteen studies were reviewed in detail,[8,16–28] resulting in exclusion of 4 studies for reporting short-term outcomes of the same trials and 1 trial evaluating a biodegradable-polymer everolimus DES.[25–28] Thus, a total of 9 trials involving 17 682 patients were included in the current analysis (Figure 1).[8,16–24] All included trials were multicenter. Cobalt chromium–based everolimus DES (Promus, Boston Scientific, Natick, MA; and Xience, Abbott Vascular, Santa Clara, CA) were used predominantly in most trials, except for 1 trial[19] that had 50% cobalt chromium–based everolimus DES and 50% cobalt-based phosphorylcholine zotarolimus DES (Endeavor; Medtronic, Minneapolis, MN) and another 2 trials that had 100% Endeavor DES implanted.[17,22] The primary outcome of MACE was defined as the composite of death, MI, or TVR, except for the NORSTENT trial[8] (defined as death or MI), the Xience or Vision Stents for the Management of Angina in the Elderly (XIMA) trial[18] (defined as death, MI, stroke, TVR, or major bleeding), and the Everolimus-Eluting Stent vs Bare-Metal Stent in ST-Segment Elevation Myocardial Infarction (EXAMINATION) trial[20]

TABLE 1 Baseline study characteristics of the included trials

Study/First Author	Year	Single/ Multicenter	Tested Device	DES Device	Control Device	Follow-up Duration, mo	Total Patients, DES/BMS	Follow-up Completion, %	Recommended Duration of DAPT, mo[a]	Primary Outcome
NORSTENT[8]	2016	Multicenter	EES (83%), ZES (13%)	Promus (66.8%), Xience V (15.5%), Endeavor Resolute (11.1%)	BMS—Driver (42.8%), Integrity (22%), Liberte (18%), Multi-Link Vision (18%)	59	4504/4509	99	9	Composite of death from any cause and nonfatal spontaneous MI at a median follow-up of 5 years
Remkes et al[16]	2016	Multicenter	EES	Xience V	BMS	24	234/240	95	12	MLD at 9-month follow-up angiography
ZEUS[17]	2015	Multicenter	ZES	Endeavor	BMS (Tsunami, Skylor, Integrity, Multi-Link Vision, and Avant-Garde)	12	802/804	100	1	1-year MACE, which included death, MI, or TVR
XIMA[18]	2014	Multicenter	EES	Xience V	BMS (Multi-Link Vision)	12	399/401	100	12	1-year composite of death, MI, stroke, TVR, or major hemorrhage
PRODIGY[19]	2014	Multicenter	ZES (50%), EES (50%)	Endeavor (50%), Xience V (50%)	BMS	24	1001/502	100	6 or 24	2-year outcome of MACE, which included death of any cause, nonfatal MI, or TVR
EXAMINATION[20]	2016	Multicenter	EES	Xience V	BMS (Multi-Link Vision)	60	751/747	97	12	All-cause death, MI, revascularization at 1 year
BASKET-PROVE[21]	2010	Multicenter	EES	Xience V	BMS	24	774/765	96	12	Composite of death from cardiac causes or nonfatal MI at 2 years
ENDEAVOR II[22]	2010	Multicenter	ZES	Endeavor	BMS	60	597/596	97	3	Target-vessel failure
SPIRIT FIRST[23]	2010	Multicenter	EES	Xience V	BMS (Multi-Link Vision)	60	27/29	88	3	In-stent late loss

Abbreviations: BASKET-PROVE, Basel Stent Kosten Effektivitäts Trial–Prospective Validation Examination; BMS, bare-metal stents; DAPT, dual antiplatelet therapy; EES, everolimus-eluting stents; ENDEAVOR II, Medtronic Endeavor Drug-Eluting Coronary Stent System in Coronary Artery Lesions; EXAMINATION, Everolimus-Eluting Stents vs Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction; MACE, major adverse cardiovascular events; MI, myocardial infarction; MLD, minimal luminal diameter; NORSTENT, Norwegian Coronary Stent trial; PRODIGY, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study; SPIRIT FIRST, prospective, single-blind, randomized, multicenter trial comparing outcomes in patients treated with Xience V/Promus vs BMS; TVR, target-vessel revascularization; XIMA, Xience or Vision Stents for the Management of Angina in the Elderly; ZES, zotarolimus-eluting stents; ZEUS, Zotarolimus-Eluting vs Bare-Metal Stents in Uncertain Drug-Eluting Stent Candidates.

[a] Recommended duration of DAPT in both DES and BMS arms in months.

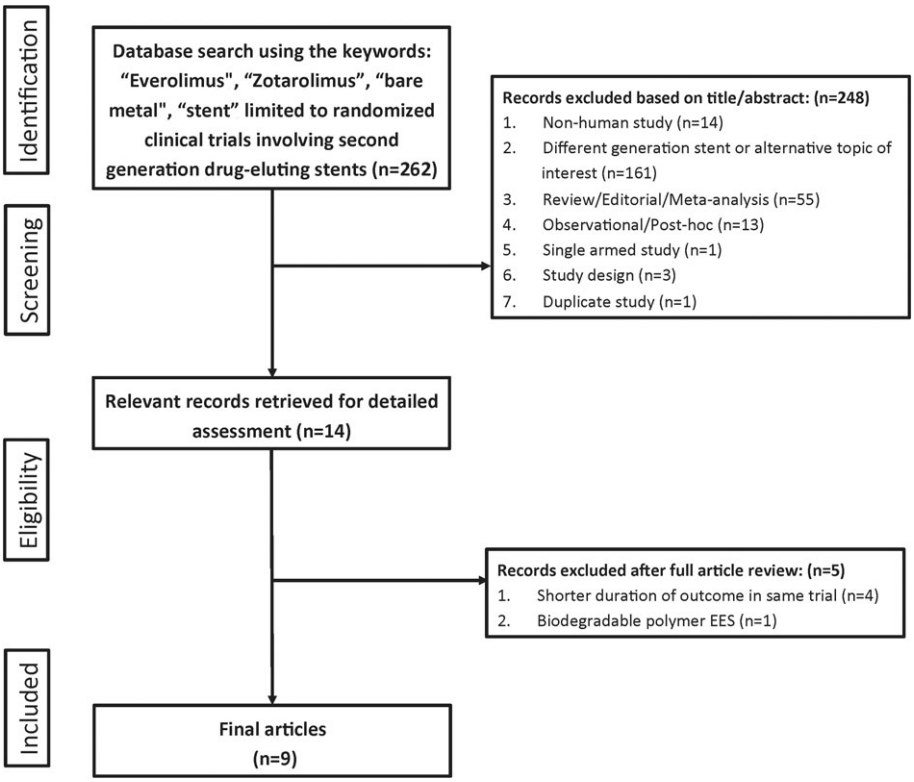

FIGURE 1 Search strategy and selection criteria (PRISMA) figure. Abbreviations: EES, everolimus-eluting stent; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

(defined as death, MI, and any revascularization). All trials reported MI as any infarction (ie, periprocedural or spontaneous) except NORSTENT,[8] which reported spontaneous and periprocedural MI separately. We opted to use all MI events for the NORSTENT trial (both periprocedural and spontaneous) for the definition of MI to be homogenous between all studies when calculating the MI outcome summary effect size. The mean follow-up completion for all trials was good, with overall follow-up completion of 98.5%. Most of the patients were males (weighted average, 75%) with a weighted mean age of 65.3 years (SE, 0.04). The recommended duration of DAPT varied between trials (1–12 months); this was the same in both DES and BMS groups, except in the XIMA trial, which recommended 1 month of DAPT for patients receiving BMS and 12 months for patients receiving DES.[18] The patients' compliance on DAPT was only reported in 5 trials,[17–21] and it was also similar between both groups in the reported trials (see Supporting Information, Table 2, in the online version of this article). Table 1 illustrates the studies and patients' characteristics of the included trials, and Table 2 illustrates the patients' demographics of the included trials.

3.2 | Studies and outcomes quality assessment

At the studies level, most trials had low evidence of bias by the Cochrane tool (see Supporting Information, Figure 1, in the online version of this article). Also, the level of evidence was strong for both primary outcomes assessed by the GRADE tool (see Supporting Information, Table 3, in the online version of this article).

3.3 | Primary efficacy outcome (MACE)

All trials reported the primary outcome of MACE. At a mean follow-up of 45.7 months, DES was associated with lower incidence of MACE compared with BMS (17.3%, 95% CI: 13.7%-20.8% vs 22.3%, 95% CI: 18.6-26.2%; RR: 0.78, 95% CI: 0.69-0.88, $P < 0.0001$, $I^2 = 66\%$; Figure 2). Such high degree of heterogeneity was not evident after exclusion of trials with different MACE definitions[8,18,20] (RR: 0.72, 95% CI: 0.64-0.81, $P < 0.0001$, $I^2 = 23\%$; see Supporting Information, Figure 2, in the online version of this article). Sensitivity analysis after exclusion of the trial with different DAPT duration in both arms[18] showed similar results (RR: 0.78, 95% CI: 0.68-0.89, $I^2 = 69\%$, $P < 0.0001$). Meta-regression analyses failed to show any effect modification by age, percentage of LAD involvement, and percentage of patients with DM in the DES arm (see Supporting Information, Figures 3–5, in the online version of this article). Subgroup analysis by DES stent type showed similar results in both everolimus-eluting stents and zotarolimus-eluting stents (see Supporting Information, Figure 6, in the online version of this article). There was no evidence of publication bias by the Egger test ($P = 0.11$; see Supporting Information, Figure 7, in the online version of this article).

3.4 | Primary device safety outcome (stent thrombosis)

All trials except 2 reported the outcome of definite stent thrombosis.[18,19] At a mean follow-up of 47.3 months, DES was associated with lower incidence of definite stent thrombosis compared with BMS (0.7%, 95% CI: 0.4%-1.0% vs 1.5%, 95% CI: 1.0%-2.1%; RR: 0.57, 95% CI: 0.41-0.78, $P < 0.0001$, $I^2 = 0\%$; Figure 2). Subgroup analysis by DES stent type showed similar results (see Supporting Information, Figure 8, in the online version of this article). The incidence of definite/probable stent thrombosis was lower with DES as well (RR: 0.54, 95% CI: 0.38-0.80, $P = 0.02$, $I^2 = 0\%$; see Supporting Information, Figure 9, in the online version of this article). There was

TABLE 2 Baseline characteristics of individuals enrolled in the clinical trials

Study/First Author	Mean Age, y, DES/BMS	Male Sex, %, DES/BMS	DM, %, DES/BMS	Prior MI, %, DES/BMS	Stable Angina, %, DES/BMS	UA, %, DES/BMS	Silent Ischemia, %, DES/BMS	NSTEMI, %, DES/BMS	STEMI, %, DES/BMS	LAD, %, DES/BMS	LCX, %, DES/BMS	RCA, %, DES/BMS	ACC/AHA B2-C[a], %, DES/BMS
NORSTENT[8]	63/63	75/75	13/12	10/11	29/29	13/12	NR	31/32	27/26	NR	NR	NR	49/47
Remkes et al[16]	66/65	75/73	19/17	16/14	0/0	0/0	0/0	100/100	0/0	40/37	26/26	26/28	80/83
ZEUS[17]	72/72	70/71	27/26	24/24	37/37	17/16	NR	27/28	19/19	53/51	33/35	42/39	73/73
XIMA[18]	84/83	60/59	26/24	30/22	NR	NR	NR	NR	0/0	61/63	32/30	38/35	NR
PRODIGY[19]	68/69	77/74	24/24	27/23	26/24	19/19	NR	22/23	33/34	58/58	34/29	36/38	66/63
EXAMINATION[20]	61/62	84/82	18/16	4/6	0/0	0/0	0/0	0/0	100/100	42/39	14/15	42/45	NR
BASKET-PROVE[21]	66/66	76/77	15/14	11/13	35/37	32/34[b]	NR	32/34[b]	31/31	53/52	26/27	40/42	NR
ENDEAVOR II[22]	62/62	77/75	18/22	40/42	NR	NR	NR	NR	NR	43/48	22/21	34/31	NR
SPIRIT FIRST[23]	64/61	70/76	11/10	24/14	78/79	19/14	3/7	NR	NR	48/45	22/21	30/34	59/62

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; BASKET-PROVE, Basel Stent Kosten Effektivitäts Trial–Prospective Validation Examination; BMS, bare-metal stent; DM, diabetes mellitus; ENDEAVOR II, Medtronic Endeavor Drug-Eluting Coronary Stent System in Coronary Artery Lesions; EXAMINATION, Everolimus-Eluting Stents vs Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction; LAD, left anterior descending coronary artery lesion; LCX, left circumflex coronary artery lesion; MI, myocardial infarction; NORSTENT, Norwegian Coronary Stent trial; NR, not reported; NSTEMI, non–ST-segment elevation myocardial infarction; PRODIGY, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study; RCA, right coronary artery lesion; SPIRIT FIRST, prospective, single-blind, randomized, multicenter trial comparing outcomes in patients treated with Xience V/Promus vs BMS; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina; XIMA, Xience or Vision Stents for the Management of Angina in the Elderly; ZEUS, Zotarolimus-Eluting vs Bare-Metal Stents in Uncertain Drug-Eluting Stent Candidates.

[a] B2-C: Classification of the coronary artery lesions according to the ACC/AHA.

[b] UA and NSTEMI.

no evidence of publication bias by the Egger test (P = 0.96; see Supporting Information, Figure 10, in the online version of this article).

3.5 | Secondary outcomes

Compared with BMS, DES was associated with lower incidences of MI (RR: 0.67, 95% CI: 0.48-0.95, P = 0.02, I^2 = 70%) and TLR (RR: 0.47, 95% CI: 0.42-0.53, P < 0.0001, I^2 = 0%). However, the incidence of all-cause mortality was similar between both arms (RR: 0.94, 95% CI: 0.79-1.10, P = 0.47, I^2 = 39%; Figure 3). On further meta-regression analyses, DES implantation in patients with older age (RR: 0.69, 95% CI: 0.50-0.96, P = 0.026 for every 10-year increase in age; see Supporting Information, Figure 11, in the online version of this article) and patients with DM (RR: 0.58, 95% CI: 0.44-0.75, P < 0.0001 per 10% increase in DM patients in each trial; see Supporting Information, Figure 12, in the online version of this article) was associated with lower incidences of MI compared with BMS.

4 | DISCUSSION

The current analysis demonstrated that second-generation DES (ie, everolimus- and zotarolimus-eluting stents) had improved clinical efficacy and device safety outcomes compared with BMS. There was a 22% reduction in MACE and a 43% reduction in definite stent thrombosis. The reduction in MACE was mainly driven by a 33% reduction in MI and a 53% reduction in TLR with second-generation DES compared with BMS.

Previous RCTs had shown an improvement in device safety outcomes (ie, definite stent thrombosis) with second-generation DES but failed to show a consistent benefit in hard clinical outcomes, such as all-cause mortality and MI. In the recently conducted NORSTENT trial involving 9013 patients, investigators did not find a difference in the composite of all-cause mortality and nonfatal MI at 6-year follow up between second-generation DES and BMS, though there was a significant reduction in rates of repeat revascularization and definite stent thrombosis.[8] However, in EXAMINATION,[26] the primary outcome of composite of all-cause mortality, recurrent MI, or repeat revascularization at 5-year follow up[20] was significantly lower, with evidence of less target-vessel MI and all-cause mortality with DES. In the Basel Stent Kosten Effektivitäts Trial–Prospective Validation Examination (BASKET-PROVE),[21] involving 2314 patients undergoing PCI, the investigators did not detect a difference between second-generation DES and BMS in rates of death or MI and definite stent thrombosis at 2 years of follow-up, although they found a lower rate of TVR in the group receiving DES. These trials were probably underpowered to detect a difference in clinical outcomes such as MI, a limitation that was overcome by the current meta-analysis. It is worth noting that PCI of saphenous venous grafts has been associated with worse outcomes as compared with native coronary arteries,[29] and randomized trials to date have failed to show any difference in outcomes between BMS and DES for PCI of saphenous vein grafts.[30]

First-generation DES showed a reduction in stent restenosis and TVR compared with BMS,[31,32] but there were concerns regarding increased late and very late stent thrombosis.[4] Second-generation DES

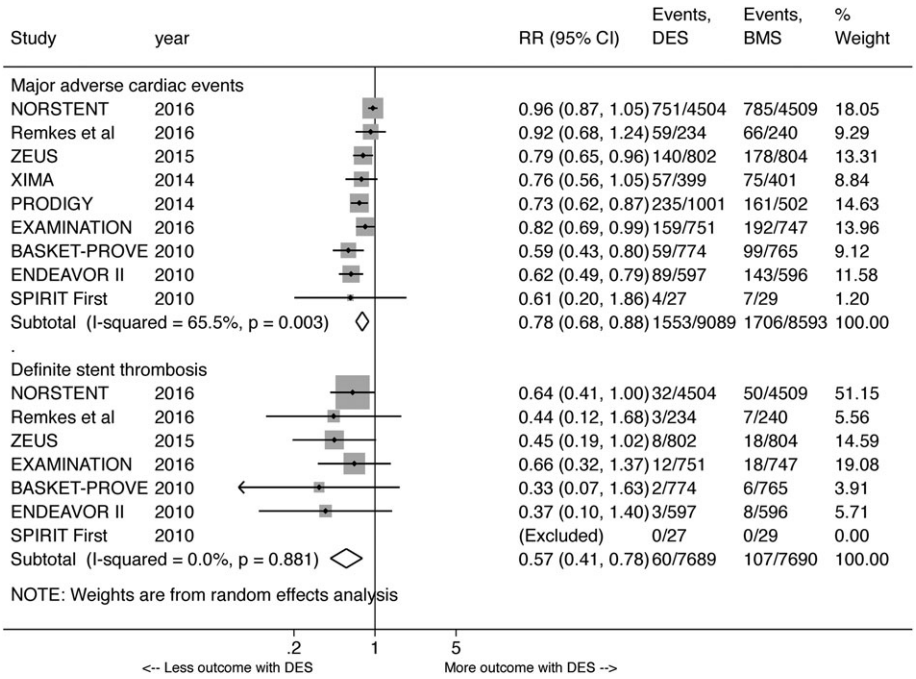

FIGURE 2 Summary risk ratio of MACE and definite stent thrombosis. The relative size of the data markers indicates the weight of the sample size from each study. *P* value represents χ^2 test of heterogeneity. Abbreviations: BASKET-PROVE, Basel Stent Kosten Effektivitäts Trial–Prospective Validation Examination; BMS, bare-metal stents; CI, confidence interval; DES, drug-eluting stents; ENDEAVOR II, Medtronic Endeavor Drug-Eluting Coronary Stent System in Coronary Artery Lesions; EXAMINATION, Everolimus-Eluting Stents vs Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction; MACE, major adverse cardiac events; NORSTENT, Norwegian Coronary Stent trial; PRODIGY, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study; RR, risk ratio; SPIRIT FIRST, prospective, single-blind, randomized, multicenter trial comparing outcomes in patients treated with Xience V/Promus vs BMS; XIMA, Xience or Vision Stents for the Management of Angina in the Elderly; ZEUS, Zotarolimus-Eluting vs Bare-Metal Stents in Uncertain Drug-Eluting Stent Candidates

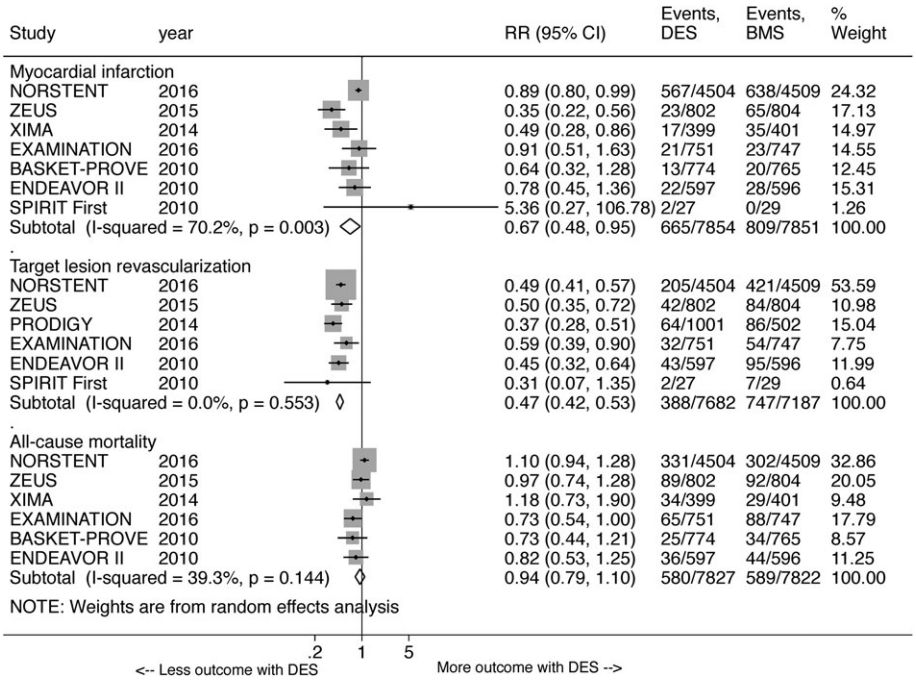

FIGURE 3 Summary risk ratios of MI, TLR, and all-cause mortality (secondary efficacy outcomes). The relative size of the data markers indicates the weight of the sample size from each study. *P* value represents χ^2 test of heterogeneity. Abbreviations: BASKET-PROVE, Basel Stent Kosten Effektivitäts Trial–Prospective Validation Examination; BMS, bare-metal stents; CI, confidence interval; DES, drug-eluting stents; ENDEAVOR II, Medtronic Endeavor Drug-Eluting Coronary Stent System in Coronary Artery Lesions; EXAMINATION, Everolimus-Eluting Stents vs Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction; MI, myocardial infarction; NORSTENT, Norwegian Coronary Stent trial; PRODIGY, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study; RR, risk ratio; SPIRIT FIRST, prospective, single-blind, randomized, multicenter trial comparing outcomes in patients treated with Xience V/Promus vs BMS; TLR, target-lesion revascularization; XIMA, Xience or Vision Stents for the Management of Angina in the Elderly; ZEUS, Zotarolimus-Eluting vs Bare-Metal Stents in Uncertain Drug-Eluting Stent Candidates

have thinner struts and thinner, more biocompatible polymers, which helped improve the device safety endpoints of stent thrombosis and restenosis.[26] Optical coherence tomography studies have demonstrated that after primary PCI for ST-segment elevation MI, the rate of uncovered struts and stent malapposition was higher for first-generation DES compared with BMS,[33] and similar for second-generation DES and BMS.[34] This can explain the improved stent thrombogenicity of second-generation DES compared with first-generation DES.

To our knowledge, this meta-analysis is the first to demonstrate a lower incidence of MI with second-generation DES compared with BMS in older patients and those with LAD lesions undergoing PCI. This is consistent with prior evidence from subgroup analyses of RCTs and registry databases that showed improved outcomes with DES in elderly patients[35–37] and patients with DM.[38]

At present, >70% of patients undergoing PCI receive a DES.[39] A DAPT of 4 weeks is generally recommended for BMS, compared with 6 to 12 months for DES[40]; hence, BMS are classically the stents of choice for patients at high risk of bleeding or those unable to adhere to DAPT[41] to avoid stent thrombosis. The current analysis shows that both device safety and patient clinical outcomes are improved by second-generation DES compared with BMS and therefore should be considered more strongly during PCI. It also raises a question regarding the feasibility of shorter DAPT duration with the newer second-generation DES. A recent study[17] demonstrated that a truncated course of DAPT—as short as 30 days—resulted in superior outcomes with second-generation DES compared with BMS with a reduction in MI, TVR, and stent thrombosis. This suggests that even in patients with concerns regarding adherence to DAPT or those with bleeding concerns, second-generation DES can be considered over BMS. There are also disparities regarding the use of DES based on race, ethnicity, and insurance status.[39,42] This disparity in the use of DES could be partially related to a lack of provider awareness regarding the increased safety of second-generation DES over BMS, in addition to residual concerns regarding the safety of first-generation DES.[43]

4.1 | Study limitations

There are certain limitations with our analysis. First, the definition of MACE was different in different studies; thus, we conducted a sensitivity analysis after excluding trials with different definitions to decrease the heterogeneity between the studies. Second, we could not assess if there was a difference in outcomes related to acute coronary syndrome or non–acute coronary syndrome indications for PCI, as this was not indicated in most of the included studies. Third, the differential duration of DAPT between DES and BMS was reported in only 4 of 9 included trials, which could confound outcomes. Finally, as the data were analyzed at trial levels, it was not possible to assess if all the baseline characteristics were balanced among the groups.

5 | CONCLUSION

Compared with BMS, second-generation DES appear to have a better safety and efficacy profile with lower incidence of MACE, MI, TLR, and stent thrombosis.

Conflicts of interest

Dr. Anderson is a consultant for Biosense Webster, a Johnson & Johnson Company. Dr. Bavry discloses an honorarium from the American College of Cardiology. The authors declare no other potential conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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